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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/775,648	02/05/2001	Toshiaki Takezawa	202785US0X	3290

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EXAMINER

MARVICH, MARIA

ART UNIT PAPER NUMBER

1636

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/775,648

Applicant(s)

TAKEZAWA ET AL.

Examiner

Maria B Marvich, PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 February 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-6,8,9,12,14-16,21,23,27,29-31,34 and 35 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4-6,8,9,12,14-16,21,23,27,29-31,34 and 35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- 1) ☒ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

This office action is in response to an amendment filed 2/16/04. Claims 1-3, 7, 10-11, 13, 17-20, 22, 24-26, 28, 32-33 and 36 have been cancelled. Claims 4-6, 8, 12, 14-16, 21 and 34-35 have been amended. Claims 4-6, 8, 9, 12, 14-16, 21, 23, 27, 29-31 and 34-35 are pending in this application.

Response to Amendment

Any rejection of record in the previous action not addressed in this office action is withdrawn. There are new grounds of rejection herein that were not necessitated by applicant's amendment and therefore, this action is not final.

Claim Objections

Claims 12, 14-16 and 21 are objected to because of the following informalities: the claims recite in line 12 that "the cells obtained from animals is". The term "is" should be substituted with the word "are". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-6, 8, 9, 12, 14-16, 21, 23, 27, 29-31 and 34-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **These are new rejections.**

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Claims 4-6, 8, 9, 12, 14-16, 21, 23, 27, 29-31 and 34-35 are vague and indefinite in that the metes and bounds of the word “substitute” are unclear. It is unclear how tissue can “substitute” a function. Tissue is a structure that performs functions but is not itself a function.

Claims 4-6, 8, 9, 12, 14-16, 21, 23, 27, 29-31 and 34-35 are vague and indefinite in that the metes and bounds of the term “to implant a fertilized ovum” are unclear. It is unclear how a tissue can “implant a fertilized ovum” as this is an active step whereas the tissue functions as a scaffold and can’t physically perform such a function. Furthermore, in vivo, the egg is implanted in the uterus but as recited in the claims, it is unclear to what the egg is implanted.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 4-6, 12, 15 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spaulding et al (US patent 6,001,643; see entire document) in view of Schinstine et al (US 5,840,576; see entire document). **This is a new rejection.**

Applicants claim a co-culturing carrier for co-culturing a fertilized ovum of an animal comprising a cell-incorporated type three-dimensionally reconstructed tissue in which the cells are pretreated with mitomycin C. The carrier further comprises extracellular matrix such as Collagen I and/or a mesh network. The specification teaches that the mesh network is not

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particularly limited so long as it can form a spatial shape for three-dimensional culturing (see page 10, line 1-3). In some instances, the mesh network is limited to gauze or cotton.

Spaulding et al teach use of a hydrodynamic cell culture environment comprised of a tissue culture chamber for three-dimensional tissue growth (abstract and column 9, line 44-57). As a general method, tissue is introduced into a roller bottle that is constructed of material suitable for cell and tissue culture i.e. polystyrene, nylon and the like (column 7, line 20-30). Cells are suspended in media in the chamber and as the cells aggregate, they form an autologous extracellular matrix upon which cells adhere, differentiate and become 3-dimensional tissue (column 14, line 61–column 15, line 1). Specifically for use in developing embryos, Spaulding et al teach co-culturing of a fertilized ovum of an animal with endometrial tissue in the chamber. Therefore, the carrier of Spaulding et al comprises a scaffold (endometrial tissue) for the cellular growth of a fertilized egg once it is implanted. Spaulding teaches that the endometrial tissue (which is comprised of epithelial cells and stromal cells) is co-cultured with the fertilized egg such that endometrial implantation constructs are formed that support endometrial maturation until it is transplanted into a recipient uterus (example 8, column 20, line 29-56).

Spaulding et al do not teach use of mitomycin pretreated cells or an extracellular matrix such as collagen I or a mesh network as part of the co-culturing carrier.

Schinstine et al teach use of mitomycin C to control cell growth of dividing cells so that a supply of differentiated cells is generated (see e.g. column 7, line 44-52 and column 13, line 23-31). Furthermore, extracellular matrix proteins alone or in combination with a physical matrix or other growth controlling substance (see e.g. column 14, line 33-39) are used to decrease

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proliferation and increase differentiation (see e.g. column 15, line 11-22). The extra cellular matrix is gelled and includes collagen I (see e.g. example 4, page 24).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate into the co-culturing carrier taught by Spaulding et al the extracellular matrix or mitomycin C taught by Schinstine et al because Spaulding et al teach that it is within the ordinary skill of the art to develop a scaffold comprised of differentiating endometrial cells for the co-culturing of a fertilized ovum and because Schinstine et al teach that it is within the ordinary skill of the art to culture cells for tissue engineering in the presence of mitomycin C or with extra cellular matrix. One would have been motivated to do so in order to receive the expected benefit of decreased proliferation and increased differentiation which is desired in the generation of engineered tissue (see Schinstine et al, column 15, line 11-22). Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 8-9, 12, 14-16, 23, 29-31 and 34-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spaulding et al (US patent 6,001,643; see entire document) in view of Takezawa et al (US 2003/0086423; see entire document) or Kumar (US 2003/0064089; see entire document). **This is a new rejection.**

Applicants claim a co-culturing carrier for co-culturing a fertilized ovum of an animal comprising a cell-incorporated type three-dimensionally reconstructed tissue in which the cells

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are pretreated with mitomycin C. The carrier further comprises extracellular matrix such as Collagen I and/or a mesh network. The specification teaches that the mesh network is not particularly limited so long as it can form a spatial shape for three-dimensional culturing (see page 10, line 1-3). In some instances, the mesh network is limited to gauze or cotton.

The teachings of Spaulding et al are described above and are applied as before except; Spaulding et al do not teach use of a mesh network such as cotton or gauze or a biosorptive mesh network.

Takezawa et al teach use of sterilized gauze immersed in vitrified type I collagen gel which is said to have satisfactory elastic strength and serves as a cell culture substratum for developing three-dimensionality for tissue development (see e.g. page 1, paragraph 0004) and provides easy preparation for culturing and an excellent expediency (see e.g. page 1, paragraph 0023 and page 2, paragraph 0029).

Kumar teaches construction of cellulose scaffolds for use in drug delivery and tissue engineering (see e.g. abstract). Microbial cellulose has a network structure in which fine ribbon-shaped fibers composed of highly crystalline and uniaxially oriented crystalline cellulose entangle one another (see e.g. page 1, paragraph 0005). These membranes are biodegradable and have interconnected pore networks (see e.g. page 1, paragraph 0007-0008).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate into the co-culturing carrier taught by Spaulding et al the gauze immersed type I collagen gel taught by Takezawa et al or the microbial cellulose taught by Kumar because Spaulding et al teach that it is within the ordinary skill of the art to develop a scaffold comprised of differentiating endometrial cells for the co-culturing of a fertilized ovum

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and because Takezawa et al teach that it is within the ordinary skill of the art to culture cells for tissue development in gauze immersed type I collagen gel and Kumar teaches that it is within ordinary skill of the art to culture cells for tissue engineering in a mesh network composed from microbial cellulose. One would have been motivated to do so in order to receive the expected benefit of a cell culture substratum with easy preparation for culturing and excellent expediency (see e.g. page 1, paragraph 0023 and page 2, paragraph 0029) or for the benefit of flexible structures with good mechanical strength that are biodegradable and biocompatible such that they can be safely implanted in a body (see Kumar, page 1, paragraph 0007-0015). Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Spaulding et al (US patent 6,001,643; see entire document) in view of Goff and Smith (Theriogenology, 1998, 49:1021-1030; see entire document). **This is a new rejection.**

Applicants claim a co-culturing carrier for co-culturing a fertilized ovum of an animal comprising a cell-incorporated type three-dimensionally reconstructed tissue comprised of bovine endometrial epithelial or stromal cells.

The teachings of Spaulding et al are described above and are applied as before except;

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Spaulding et al do not teach use of bovine endometrial epithelial or stromal cells.

Goff and Smith teach use of Bovine endometrial cells for Co-culture after IVF (see abstract). The Bovine endometrial cells were able to maintain the embryo development to blastocyte stage (see e.g. page 1027, paragraph 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate into the co-culturing carrier taught by Spaulding et al the bovine endometrial cells taught by Goff and Smith because Spaulding et al teach that it is within the ordinary skill of the art to develop a carrier for the co-culturing of a fertilized ovum comprised of endometrial cells and because Goff and Smith teach that it is within the ordinary skill of the art to co-culture an embryo with Bovine endometrial cells. One would have been motivated to do so in order to receive the expected benefit that bovine cells are readily available for purchase, can survive at least 10 doublings and maintain embryo development to the blastocyte stage (see Call Application on line catalog and Goff and Smith page 1027, paragraph 1). Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

No Claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

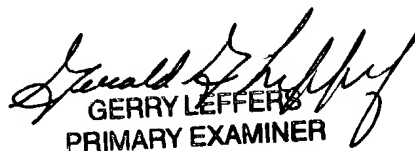
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
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April 22, 2004


GERRY LEFFERS
PRIMARY EXAMINER